

Application No.: 10/570,117

Reply to Restriction Requirement dated April 17, 2007

In response to Examiner's Restriction Requirement dated January 18, 2008

Amendments to the Claims

This listing of claims will replace all prior versions and listings in this application.

Listing of Claims

1. **(Original)** A gene construct comprising a reporter gene operably linked to a promoter containing a transcriptional regulatory element that is up-regulated by a transcription factor preferentially produced in neoplastic cells.
2. **(Original)** The gene construct of claim 1, wherein the transcriptional regulatory element is selected from the group consisting of a beta-catenin response element, an E2F response element, a Forkhead response element, and a Smad-2/Smad-3 response element.
3. **(Original)** The gene construct of claim 1, wherein the reporter gene encodes a protein selected from the group consisting of an enzyme, a bioluminescent protein, and a fluorescent protein.
4. **(Original)** The gene construct of claim 3, wherein the enzyme is selected from the group consisting of .beta.-galactosidase, alkaline phosphatase, and chloramphenicol acetyltransferase.
5. **(Original)** The gene construct of claim 3, wherein the bioluminescent protein is a luciferase.
6. **(Original)** The gene construct of claim 3, wherein the fluorescent protein is selected from the group consisting of green fluorescent protein, yellow fluorescent protein, enhanced yellow fluorescent protein, red fluorescent protein and blue fluorescent protein.
7. **(Original)** A cell comprising the gene construct of any one of claims 1-6.
8. **(Original)** The cell of claim 7, wherein the cell is an embryonic stem cell.
9. **(Currently amended)** A ~~nonhuman mammal comprising the cell of claim 7 mouse having incorporated in its genome a gene construct comprising a reporter gene operably linked to a~~

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promoter containing a transcriptional regulatory element that is up-regulated by a tumor-induced transcription factor, said mouse further comprising a neoplastic transformation-promoting genetic modification.

10. **(Cancelled)**.

11. **(Original)** A method of detecting a neoplasia a nonhuman mammal, comprising

(a) providing a nonhuman mammal, at least some of whose somatic cells are engineered cells comprising a genome comprising a neoplastic transformation-promoting genetic modification and a reporter gene operably linked to a transcriptional regulatory element wherein the transcriptional regulatory element is up-regulated by a transcription factor preferentially produced in neoplastic cells;

(b) allowing time for neoplastic transformation to occur in at least one of the engineered cells, and

(c) detecting a signal from the reporter gene expressed in the engineered cells.

12. **(Currently amended)** The method of claim 711, wherein the nonhuman mammal is a mouse.

13. **(New)** The mouse of claim 9, wherein the transcriptional regulatory element is selected from the group consisting of a beta-catenin response element, an E2F response element, a Forkhead response element, and a Smad-2/Smad-3 response element.

14. **(New)** The mouse of claim 9, wherein the reporter gene encodes a protein selected from the group consisting of an enzyme, a bioluminescent protein and a fluorescent protein.

15. **(New)** The mouse of claim 14, wherein the enzyme is selected from the group consisting of beta-galactosidase, alkaline phosphatase, and chloramphenicol acetyltransferase.

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16. **(New)** The mouse of claim 14, wherein the bioluminescent protein is a luciferase.
17. **(New)** The mouse of claim 14, wherein the fluorescent protein is selected from the group consisting of green fluorescent protein, yellow fluorescent protein, enhanced yellow fluorescent protein, red fluorescent protein and blue fluorescent protein.
18. **(New)** The mouse of claim 9, wherein the neoplastic transformation-promoting genetic modification is selected from the group consisting of an activated oncogene, an inactivating tumor suppressor gene and an inactivating DNA repair gene.
19. **(New)** The mouse of claim 18, wherein the oncogene is under the control of an inducible transcriptional system.
20. **(New)** The mouse of claim 19, wherein the inducible transcriptional system is selected from the group consisting the Cre-Lox system, the tetracycline transactivator system, reverse tetracycline transactivator system, ecdysone system, methallothionin system, LacO/IPTG system and TetO/tetracycline system.
21. **(New)** The mouse of claim 20, wherein the inducible transcriptional system is the reverse tetracycline transactivator system.
22. **(New)** The mouse of claim 18, wherein the oncogene is selected from the group consisting of myc and ras.
23. **(New)** The mouse of claim 18, wherein the tumor suppressor is selected from the group consisting of INK4a, P53, APC, PTEN, Rb, DPC4, KLF6, GSTP1, ELAC2/HPC2 and NKX3.1.
24. **(New)** The mouse of claim 18, wherein the DNA repair gene is selected from the group consisting of MSH2, MSH6, PMS2, Ku70, Ku80, DNA/PK, ATR, ATM, XRCC4 and MLH1.